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SUGHRUE MION, PLLC			HADDAD, MAHER M	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/568,761	WATANABE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 09 March 2010.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 19,20 and 31-35 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 19, 20 and 31-35 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____ .                        |

## DETAILED ACTION

1. Claims 19, 20 and 31-35 are pending and under examination in the instant application.
2. In view of the pre-appeal conference decision, dated 3/25/2010, the prosecution is reopened to new grounds of rejections. In view of the new grounds of rejection presented below, the present Office Action is made NON-FINAL. Applicant's arguments made in the Pre-Appeal Brief will be addressed as they pertain to the 102 rejections.
3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --  
*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*
4. Claims 19-20, 32 and 35 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S Pat. No. 6,423,501 OR WO/ 98/25647.

Given the shared disclosure of the WO/ 98/25647 publication and US Pat. No. 6,423,501, this rejection is made using the teachings of the US. Pat. No. 6,423,501.

The '501 patent teaches a method of treating inflammatory condition in a mammal such as human (patient) comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 13, lines 34-45 in particular). The '501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see col., 9, line 65 to col., 10, line 3 in particular). The '501 patent further teaches that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B). The functional properties claimed in claim 32 are inherent.

While the prior art teachings may be silent as to the "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties. It is noted that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169) USPQ 226 (CCPA 1971)). Therefore, in the absence of evidence to the contrary, the anti-CD81 antibody administered by

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the '501 patent, would "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method".

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference anti-CD81 antibody does not "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method" recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980). The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 03/09/2010, have been fully considered, but have not been found convincing.

Applicant points to the legal standards for anticipation and points to the court in *Verisign*, quoting *In re Arkley*, 455 F.2d 586 (C.C.P.A. 1972), held that for anticipation, "[t]he prior art reference must clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." (Emphasis added applicants.

Applicant submits that in maintaining the rejection, the Examiner picks and chooses amongst a variety of distinct and alternative embodiments of Fleming et al., which embodiments are not directly related to each other, in an attempt to find anticipation; for example, from column 13, lines 34- 45, inflammatory bowel disease is specifically chosen from a plethora of distinct and alternative diseases, and this embodiment is combined with antibodies against anti-CD81, which are specifically chosen from column 9, line 65, to column 10, line 3; however, at no point does Fleming et al. disclose Applicants' specific combination of claim elements in a single source, or provide any teaching directly relating them to one another so as to avoid the need for impermissibly picking and choosing amongst these alternative and distinct embodiments.

Applicants submit that, in violation of the standard articulated in *Arkley*, such piecing together, in the absence of any direct relationship linking them together to prevent picking and choosing, does not represent disclosure of the claimed invention "as arranged in the claim," and thus does not constitute anticipation (emphasis added by the Examiner). To hold otherwise is to submit that disclosure of a vast genus of diseases, when combined with an accompanying disclosure of a similarly vast genus of agents, anticipates every possible combination of species that can be selected from these genera; however, Applicants submit that the mere generic disclosures of Fleming et al., on which the instant rejection is based, do not constitute disclosure with "sufficient specificity" to establish anticipation. It is well-settled that "a prior art reference that discloses a genus still does not inherently disclose all species within that broad category." *Metabolite Laboratories, Inc. v. Laboratory Corporation of America*, citing *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1262 (Fed. Cir. 1989). The relied-upon portions of Fleming et al merely disclose broad genera of diseases and agents; Fleming et al. lacks any teachings to directly relate the specific species together as arranged as in the instant claims

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without picking and choosing, nor is there any pattern of preferences that would serve to narrow the number of possible embodiments to a small number of species so that one of skill in the art would have "at once envisaged" Applicants' claimed invention from these broad genera. See *In re Petering*, 301 F.2d 676 (C.C.P.A. 1962). Moreover, as a matter of law, Applicants' specifically claimed method does not inherently flow from the generic disclosures in Fleming et al.; inherent disclosure does not negate the requirement that the selected elements be disclosed with sufficient specificity in the same way as arranged in the claim without any need for picking and choosing. See page 5, 1st full paragraph, of the Response filed February 10, 2010

Applicant's reliance on the decision in *In re Arkley*, 455 F.2d 586, 172 USPQ 524 (CCPA1972)-ref covered 230,000 cmpds, is ill placed. It is immediately apparent that the facts in this case do not involve any "need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." All the 20 diseases listed by Fleming et al patent are linked by CD81 and the inhibition of inflammatory responses associated with these disorders. Moreover, 20 disorders are very small genus of diseases and the claimed inflammatory bowel disease is taught in the Fleming et al disclosure. All that is needed to implement the disclosure of Fleming et al is to treat the inflammatory responses of IBD with anti-CD81 antibody which induces CD81-mediated signal transduction.

Applicant submits that to anticipate, the reference must enable the claimed invention; Applicants submit that the reasons proffered by the Examiner in an attempt to establish that Fleming et al. enables the presently claimed invention are in clear error. First, the Examiner purports that Fleming et al. anticipates because "a patent is an enabling reference for all that it teaches." Applicants have previously noted why this reasoning is unsound. See the paragraph bridging pages 5 and 6 of the Response filed February 10, 2010. Second, the rejection is predicated on the allegation that Fleming et al. is enabling, and anticipatory, because it does place "the public ... in possession of the claimed subject matter... [t]he reason [being] that [although] section 112 'provides that the specification must enable one skilled in the art to 'use' the invention[,] ... section 102 makes no such requirement as to an anticipatory disclosure." Applicants have also noted why this reasoning is unsound. See the paragraph bridging pages 6 and 7 of the Response filed February 10, 2010. As previously pointed out by Applicants, Fleming et al. fails to enable one of skill in the art to practice the presently claimed method, at least because one of skill in the art would have had to embark on undue experimentation to connect antibody binding to CD81 as a treatment for inflammatory bowel disease amongst the myriad of other diseases recited by Fleming et al. As Applicants have previously noted on the record, as a result of such, Fleming et al. does not place those of skill in the art, in the absence of extensive and undue experimentation, in possession of the claimed invention, as is required to sustain the rejection. See page 4, 1st full paragraph, of the Amendment filed July 30, 2009.

However, Fleming et al patent publications teach how to make and how to use the anti-CD81 antibodies in the treatment of inflammatory responses associated with inflammatory bowel

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disease. Appellants have not provided persuasive evidence that one skilled in the art would not have accepted that the anti-CD81 antibodies can be used to treat inflammatory responses associated with inflammatory bowel disease.

5. Claims 19-20, 31-32 and 35 stand rejected under 35 U.S.C. 102(b) as being anticipated by Curd et al (WO 00/67796).

Curd et al teach treatment of inflammatory bowel disease, Crohn's disease and ulcerative colitis with anti-CD81 antibody (see published claims 1, 2, 3, 6) in human (published claim 7). The various functional activities recited in the claims are inherently found in said method the method taught by Curd et al teaches in vivo administration of the same antibody recited in the claims to treat the same disease recited in the claims. Curd et al teach the claimed antibody fragments (see page 4, lines 38-40).

While the prior art teachings may be silent as to the "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties. It is noted that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169) USPQ 226 (CCPA 1971)). Therefore, in the absence of evidence to the contrary, the anti-CD81 antibody administered by the '501 patent, would "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method".

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference anti-CD81 antibody does not "shortened intestinal length is improved or treated by the method" and "wherein the loose stool or diarrhea is improved or treated by the method" recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 03/09/2010, have been fully considered, but have not been found convincing.

Applicant submits that Curd et al. fails as an anticipatory reference for essentially the same reasons as Fleming et al.; the Examiner cites to Claims 1, 2, 3, 6 and 7 in an attempt to disclose the claimed invention. Claim 2 encompasses a vast genus of alternative and distinct B-cell surface antigens, and Claim 6 recites a vast genus of alternative and distinct diseases that may be treated by antagonism of a B-cell surface antigen. Claims 2 and 6 also recite a plethora of alternative and distinct embodiments. However, at no point does Curd et al. disclose Applicants'

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specific combination of claim elements in a single source, or provide any teaching directly relating them to one another so as to avoid the need for impermissibly picking and choosing amongst these alternative and distinct embodiments. Applicants submit that, in violation of the standard articulated in Arkley, the rejection is premised on picking and choosing a specific B-cell antigen from one claim, and a specific disease from another, in the absence of any teachings to directly relate the specific B-cell antigen and disease together as arranged as in the instant claims without picking and choosing. Nor is there any pattern of preferences that would serve to narrow the number of possible embodiments to a small number of species so that one of skill in the art would have "at once envisaged" Applicants' claimed invention from these broad genera. Moreover, Applicants have pointed out why Curd et al. fails as an anticipatory reference also because it fails to enable the presently claimed method. See page 10, 1st full paragraph, of the Response filed February 10, 2010. Thus, Curd et al. does not teach the presently claimed invention, and thus the rejection is in clear error.

However, Applicant's reliance on the decision in *In re Arkley*, 455 F.2d 586, 172 USPQ 524 (CCPA1972)- ref covered 230,000 cmpds, is ill placed. It is immediately apparent that the facts in this case do not involve any "need for picking, choosing and combining various disclosures not directly related to each other by the teachings of the cited reference." All the diseases listed by Curd et al publication are linked by the B cell surface marker such as CD81 and being autoimmune diseases such as inflammatory bowel disease. There are 25 B cell surface markers recited in claim 2, and 65 autoimmune diseases. These are very small genus of diseases and B-cell surface markers. All that is needed to implement the disclosure of Curd et al is to treat the inflammatory responses of IBD with anti-CD81 antibody which antagonizes CD81 effect.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 31 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 or WO 00/67796, as applied to claims 19-20, 31-32 and 35, above, and further in view of and Owens *et al* (1994).

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The teachings of Pat. No. 6,423,501 or WO 98/25647, WO 00/67796 publication have been discussed, *supra*.

The claimed invention differs from the reference teachings only by the recitation of and Fab, F(ab')<sub>2</sub> or Fv or scFv in claim 31 and the dosage recited in claims 33-34.

Owens *et al* teach the modification of murine antibodies such as a single chain antibody, a Fab fragment, a F(ab')<sub>2</sub> fragment. Owens *et al* further teach that antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement –dependent cytotoxicity (see the entire document).

Claims 33-34 are included because it is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215,219 (CCPA 1980). Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP §§ 2144.05 part II A. The determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. The duration of treatment, the specific route of administrations and like factors are within the knowledge and expertise of the medical practitioner.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the anti-CD81 antibody taught by 6,423,501 or WO 98/25647 to Fab or F(ab')<sub>2</sub> fragments taught by Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxicity as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 03/09/2010, have been fully considered, but have not been found convincing.

Applicant submits that neither Fleming et al., WO 98/25647 nor WO 00/67796 disclose, expressly or inherently, a method of improving or treating inflammatory bowel disease

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comprising administering an anti-CD81 antibody to a patient in need thereof, and there exists nothing in these references that would incite any expectation of success in performing such a method. Owens et al. fails to rectify this deficiency. See page 11 of the Response filed February 10, 2010. Thus, even assuming *arguendo* these references were combined, those of ordinary skill in the art would not arrive at the presently claimed invention. Withdrawal of the rejection is respectfully requested.

However, Applicants have not provided persuasive evidence that one skilled in the art would not have accepted that the anti-CD81 antibodies could be used to treat inflammatory bowel disease.

8. Claims 19, 20 and 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. Patent 6,423,501 OR WO 98/25647.

Given the shared disclosure of the WO/ 98/25647 publication and US Pat. No. 6,423,501, this rejection is made using the teachings of the US. Pat. No. 6,423,501.

The '501 patent teaches a method of improving or treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction.

The reference differs from the claimed invention in that the specific process as claimed is not expressly exemplifying a patient.

However, the method, in the '501 patent, is disclosed as being suitable to treat any inflammatory condition, which, of course, includes inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 13, lines 34-45 in particular). Clearly the disclosure of the reference also encompasses "improving" inflammatory bowel disease. In addition, the '501 patent teaches that agents described herein can be any molecule which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. The reference specifically teaches that the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see col., 9, line 65 to col., 10, line 3 in particular). The '501 patent uses 50 µg/275-300g (i.e., 0.17-0.18 mg/kg) of anti-CD81 antibodies (see col., 18, lines 10-15).

Accordingly, one of ordinary skill in the art would have had a reasonable expectation of success of improving or treating inflammatory bowel disease according to the teachings of '501 by providing an anti-CD-81 antibody to a patient suffering from this disease inasmuch as the reference discloses that such agents are suitable to treat inflammatory responses associated with disorders such as inflammatory bowel disease and it discloses two specific examples of such anti-CD-81 antibodies.

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Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process taught by '501 by providing an anti-CD-81 antibody to a patient suffering from inflammatory bowel disease patient by providing specific anti-CD-81 antibodies to such a patient for the expected benefit of improving or treating the painful and distressing condition of inflammatory bowel disease. It would be conventional and within the skill of the art to easily adapt the teachings of the '501 patent to treat inflammatory bowel disease patients with an anti-CD-81 antibody.

Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to deduce from the reference teaching that the method of treating inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) works in patients.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Claims 19-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/67796 to Curd et al.

Curd et al teach treatment of inflammatory bowel disease, Crohn's disease and ulcerative colitis with anti-CD81 antibody (see published claims 1, 2, 3, 6). The various functional activities recited in the claims are taught by the method taught by Curd et al because it teaches *in vivo* administration of the same antibody recited in the claims to treat the same disease recited in the claims. Curd et al teach the claimed antibody fragments include Fab, Fab', F(ab')2 and Fv fragments (see page 4, lines 38-40). Curd teaches treating any autoimmune disease in a mammal comprising administering to the mammal a therapeutically effective amount of an antagonist which binds to a B cell surface marker (published claim 1) including CD81 (published claim 2), wherein the antagonist comprises an antibody (published claim 3) and the autoimmune disease includes inflammatory bowel disease, Crohn's disease and ulcerative colitis, the mammal is human (published claim 7). Curd et al teach a dose of substantially less than 375 mg/m<sup>2</sup> of the antibody to the mammal (published claim 15), a dose ranges from 20-25 mg/m<sup>2</sup> (see published claim 16-17).

Curd's et al teaching differs from the claimed invention by not having a working example of the claimed method.

However, it would be conventional and within the skill of the art to easily adapt the teaching of Curd to treat patients. While Curd teachings do not exemplifying patients, it would be conventional and within the preview of those skilled in the art to identify and determine the optimum treatment protocols to improve and treat the inflammatory bowel disease in patients. Further, the determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to

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the claimed invention. The duration of treatment, the specific routes of administration and like factors are within the knowledge and expertise of the medical practitioner. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP §§ 2144.05 part II A.

Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to deduce from the reference teaching that the method of treating an autoimmune disease such as inflammatory bowel disease with anti-CD81 antibody in a human taught by Curd would have had a reasonable expectation of success of improving or treating inflammatory bowel disease.

Given the examination guidelines for determining obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in *KSR International Co. v. Teleflex Inc.* 82 USPQ2d 1385 (2007) and the Examination Guidelines set forth in the Federal Register (Vol. 72, No. 195, October 10, 2007) and incorporated into the MPEP (Revision 6, September 2007), the following rationales to support rejection under 35 U.S.C. 103(a) are noted:

Curd et al teach a method of treating an autoimmune disease including inflammatory bowel disease, crohn's disease and ulcerative colitis in a mammal comprising administering to the mammal a therapeutically effective amount of an antagonist which binds to B cell surface marker (see page 2, lines 23-25 and published claims 1 and 6). Curd et al teach that the surface of a B cell which can be targeted with an antagonist which binds thereto includes CD81 (see page 2, lines 32-35 and published claim 2). Curd et al suggest methods of improving and treating autoimmune diseases by targeting a B cell surface marker with antagonist. Moreover, Curd et al teach anti-CD81 antibodies that antagonize CD81 B cell surface marker which is useful as a therapeutic agent for targeting a cell expressing the CD81 (see page 7, lines 24-26, page 23, lines 8-11 and published claims 2-3).

A) Combining prior art elements according to known methods to yield predictable results.

The rationale to support a conclusion that the claims would have been obvious is that all the claimed elements (treatment of IBD with anti-CD81 antibodies) were known in the prior art and one skilled in the art could have arrived at the claimed invention by using known methods (treatment with the antagonist) with no change in their respective functions and the combination would have yielded nothing more than predictable results of improving or treating of inflammatory bowel disease.

B) Simple substitution of one known element for another to obtain predictable results.

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Those of skill in the art would have had reason to use the anti-CD81 antibody as a substitute for the improvement and treatment of autoimmune disease including IBD, Crohn's disease and ulcerative colitis because, like the B cell surface marker antagonists taught in Curd, anti-CD81 antibodies bind to B cell surface marker and antagonize its effect would have yielded predictable results of improving or treating of inflammatory bowel disease to one of ordinary skill in the art at the time of the invention. Substituting a known element for another, to yield the known result, is obvious. See KSR, 550 U.S. at 416, 421.

C) "Obvious to try" --- choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success.

The rationale to support a conclusion that the claim would have been obvious is that a person of ordinary skill has good reason to pursue the known options (substituting one B cell surface marker antagonist for another B cell surface marker antagonist in the treatment of autoimmune disease such as IBD) within his or her technical grasp. This leads to the anticipated success of improving or treating of inflammatory bowel disease, it is likely the product not of innovation but of ordinary skill and common sense.

D) Some teachings, suggestion, or motivation in the prior art that would have lead one of ordinary skill to modify the prior art reference to arrive at the claimed invention.

Since the treatment of an autoimmune disease with B cell surface marker antagonist would have been predictable at the time of the invention, there would have been reasonable expectation of successful development of treatment method of IBD with an anti-CD81 antibody as claimed. The prior art had suggested a finite number of B cell surface markers (25 marker) and a finite number of autoimmune diseases (61 autoimmune diseases). The claims were obvious because it would have been obvious to try the known methods of treating autoimmune diseases such as inflammatory bowel disease with the B cell surface marker antagonists such as anti-CD81 antibodies, with a reasonable expectation of success. "There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." *Motorola, Inc. v. Interdigital Tech. Corp.*, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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10. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 as applied to claims 19-20 and 32 above and further in view of and Owens *et al* (1994).

The teachings of the Pat. No. 6,423,501 and WO 98/25647 publication have been discussed, *supra*.

The claimed invention differs from the reference teachings only by the recitation of and Fab, F(ab')<sub>2</sub> or Fv or scFv in claim 31.

Owens *et al* teach the modification of murine antibodies such as a single chain antibody, a Fab fragment, a F(ab')<sub>2</sub> fragment. Owens *et al* further teach that antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement –dependent cytotoxicity (see the entire document).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the anti-CD81 antibody taught by 6,423,501 or WO 98/25647 to Fab or F(ab')<sub>2</sub> fragments taught by Owens *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxicity as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

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March 25, 2010

/Maher M. Haddad/  
Primary Examiner,  
Art Unit 1644